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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,192	COLAU ET AL.	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-56,77,78 and 82-145* is/are pending in the application.

4a) Of the above claim(s) *40-56,77,78,97,98,123 and 124* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *82-96,99-122 and 125-145* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is in response to the amendment filed on 04 August 2006.

Status of claims

Claims 1-39, 57-76, and 79-81 have been cancelled. Claims 94-145 have been added. Claims 40-56, 77, 78, and 82-145 are pending, of which claims 40-56, 77, 78, 97, 98, 123, and 124 are withdrawn from consideration, as being drawn a nonelected invention or species, and claims 82-96, 99-122; 125-145 are rejected.

Objections

The objection to the specification **is withdrawn** in view of the Applicant's amendment.

Claim Rejections - 35 USC § 112

The rejection of claims 57-59, 62, 64-71, 73-76, and 79-81 under 35 U.S.C. §112, second paragraph, as being indefinite is **withdrawn** in view of the cancellation of the claims.

The rejection of claims 82-93 under 35 U.S.C. §112, second paragraph, as being indefinite is **maintained and extended to new claims 94-145**. Applicants argue that the specification defines the term, "substantially a single variant" as at least a 90% single variant. However, this definition is still not clear enough to allow one to differentiate between "a single variant" and "substantially a single variant." It is unclear

what the percentage is in reference to. This rejection can be obviated by deleting the phrase "substantially a single variant" in each claim.

Claims 82, 84, and 86 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 82, 84, and 86 all contain the phrase "encoding at least one of the major viral proteins designated as VP4 and VP7" which can mean three different compositions: (1) VP4 alone; (2) VP7 alone; or (3) VP4 and VP7. Therefore, the phrase renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). This rejection also affects all the dependent claims.

Claim Rejections - 35 USC § 102

The rejection of claims 57-59, 62, 65, 69, 71, 80, and 81 under 35 U.S.C. §102(b) as being anticipated by Burke *et al.* (US 5,932,223) is **withdrawn-in-part** in view of the cancellation of the claims **and extended to the amended claims 82-85 and new claims 95, 96, 99, 100, 113-115, 121, 122, 125, 126, and 132**. The amendments to claims 82 and 84 contain the phrase "encoding at least one of the major viral proteins designated as VP4 and VP7" so that claim 82 encompasses any VP7 without the mutational limitation and claim 84 encompasses any VP4 without the mutational limitation.

The rejection of claims 57, 58, 69, and 79-81 under 35 U.S.C. §102(e) as being anticipated by Hoshino *et al.* (US 2002/0058043) is **withdrawn-in-part** in view of the

cancellation of the claims **and extended to the amended claims 82-85 and new claims 113-115 and 139-141** because of the amendments to claims 82 and 84. See above.

Claim Rejections - 35 USC § 103

The rejection of claims 57, 58, 69, 73, and 79-81 under 35 U.S.C. §103(a) as being obvious over Hoshino *et al.* (US 2002/0058043) in view of Chen *et al.* (US 6,552,024) is **withdrawn-in-part** in view of the cancellation of the claims **and extended to the amended claims 82-85 and new claims 109 and 135** because of the amendments to claims 82 and 84. See above.

The rejection of claims 57-59, 62, 64-67, 69, 74, and 79-81 under 35 U.S.C. §103(a) as being obvious over Hoshino *et al.* (US 2002/0058043) in view of Tsutsumi *et al.* (US 4,152,421) is **withdrawn-in-part** in view of the cancellation of the claims **and extended to the amended claims 82-85 and new claims 101-104, 106, 108, 110, 112, 127-130, 134, 136, and 138** because of the amendments to claims 82 and 84. See above.

The rejection of claims 57-59, 62, 64-71, 74-76, and 79-81 under 35 U.S.C. §103(a) as being obvious over Hoshino *et al.* (US 2002/0058043) in view of Tsutsumi *et al.* (US 4,152,421) and further in view of the Therapeutic Goods Administration in the Department of Community Services and Health in Australia (1991) is **withdrawn-in-part** in view of the cancellation of the claims **and extended to the amended claims 82-85 and new claims 105, 107, 111, 131, 133, and 137** because of the amendments to claims 82 and 84. See above.

New Rejection - 35 USC § 112, written description

Claims 82-86, 89, 92-94, 116, 117, and 142 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4) *functional characteristics alone or coupled with a known or disclosed correlation between structure and function*, and the (5) *method of making the claimed invention*. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." M.P.E.P. §2163.

In the instant case, the claims are directed to a vaccine composition comprising a live attenuated human rotavirus population. Based on the definition in the specification as stated by the Applicants on page 13 in the response filed on 04 August 2006, the limitation "substantially a single variant" encompasses all variants with less than 10% mutated positions in the sequences, which can be single-mutations, multiple-mutations, including deletion, insertion, substitution. Thus, the claims are drawn to a genus of inordinate number of rotavirus species with disparate functional activities.

M.P.E.P. § 2163 states that, if the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. The length of VP4 gene is 2350 bp. The length of VP7 gene is 1009 bp. A 10% variance in each antigen would be up to 235 bp difference in VP4 region and up to 101 bp difference in VP7 region. The specification only provides description for variations at 3 positions in VP4 and VP7 regions in rotavirus populations designated as P33, P38, and P43 (p. 16-17, Table 3), among which only P43 was demonstrated to possess the vaccine function. Thus, Applicants do not have possession of any variants other than the disclosed P33, P38, and P43.

As discussed above, the skilled artisan cannot envision the detailed chemical structure and function of the encompassed genus of undefined nucleotides. The specification lacks sufficient variety of species to reflect the 10% sequence variance in the genus. A definition by function alone "does not suffice, to sufficiently describe a coding sequence" because it is only an indication of what the gene does, rather than what it is." *Eli Lilly*, 119F.3 at 1568, 43USPQ2d at 1406.

Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the "substantially single variants" and does not reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the entire scope of the claimed invention.

Therefore, claims 82-86, 89, 92-94, 116, 117, and 142 do not meet the written description provision of 35 U.S.C. §112, first paragraph.

New Rejection - 35 USC § 112, scope of enablement

Claims 82-88, 92, 93, 95, 96, 99-119, 121, 122, 125-144 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a vaccine composition containing P43 with all six mutations present in VP4 and VP7 regions, does not reasonably provide enablement for any single or other multiple mutation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Enablement is considered in view of the *Wands* factors (MPEP §2164.01(a)).

The claims are drawn to a vaccine composition comprising a live attenuated human rotavirus population defined by a nucleotide sequence encoding at least one of VP4 and VP7, in which the VP4 or VP7 gene comprises at least one substitution. The broad claims encompass any single mutation in either VP4 or VP7 region.

The art of rotavirus vaccine development is highly uncertain and unpredictable in terms of its efficacy. The major problem with rotavirus vaccine is intussusception (Glass, 2006). Any other rotavirus variant that does not contain the six mutations in VP4 and VP7 regions as P43 has not be assessed for its efficacy and risk for clinical use.

The only working example disclosed in the specification is P43. There is no specific guidance regarding the safety and efficacy of the variants which contain only one of the mutations present in P43. A live attenuated rotavirus vaccine is not considered routine in the art and without sufficient guidance to protection against

rotavirus infection by any single point mutant, the experimentation left to those skilled in the art is undue or unreasonable under the circumstances. It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See *Ex parte Singh*, 17 USPQZd 1714 (BPAI 1991).

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed rotavirus vaccines containing less than the six mutations in P43.

New Rejection - 35 USC § 102 or 103

Claims 82-94, 116-120, and 142-145 are rejected under 35 U.S.C. § 102(e) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Hoshino *et al.* (US 2002/0058043). Hoshino *et al.* disclose cloned strain derived from human rotavirus. Particularly, the attenuated human rotavirus is produced by at least 10 serial cold passages in AGMK cells followed by plaque purification (¶35) and thus contains attenuating mutations that produce cold adapted and temperature sensitive phenotype (Abstract). The specification states that the claimed invention is isolated by 26, 33, 38, or 43 successive passages in AGMK or VERO cells and subsequent individual plaque isolation or limit dilution. There is no description of the phenotype of the claimed rotavirus populations, however, the specification further discloses that "it is not altogether impossible or improbable that similar and functionally substantially identical rotaviruses might be produced by these or other methods in view of the teachings or

this invention. Such functionally substantially identical rotaviruses are considered to be biologically equivalent to invention" (page 7). Given the instant disclose of how the claimed attenuated rotavirus population is produced (pages 5-6), the human rotavirus containing attenuated mutations disclosed in Hoshino *et al.* meet the limitations of the claims. Therefore, the claimed rotavirus with the genetic characterization must be disclosed in Hoshino *et al.* Where applicant claims a composition in terms of a characteristic not explicitly disclosed by the reference, a §102/103 rejection is proper (MPEP §2112).

Patent owner's burden under the circumstances presented herein was described in *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on 'inherency' under 35 U.S.C. §102, on 'prima facie obviousness' under 35 U.S.C. §103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior ad products (footnote omitted).

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached at 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Jeffrey Parkin, Ph.D.
Primary Examiner
14 October 2006

10/14/2006